REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims and Amendments

Claims 2, 8, 18-20, and 26 are requested to be canceled without prejudice or disclaimer.

Claims 1, 9-12, 39, 47, and 48 are requested to be amended. Claims 1, 47, and 48 are being amended to recite the subject matter of claims 8, 11, and 13. Claim 11 is being amended to remove subject matter now recited by its parent claim, claim 1. Claim 12 is being amended to take into account the amendments made to claims 1 and 11. Claims 9 and 10 are being amended to change their dependency based on the cancellation of claim 8. No new matter is being added.

After amending the claims as set forth above, claims 1, 5-7, 9-17, 21-24, and 27-46 are pending, and claims 15-17, 21-24, 29, 31-38, and 40-46 are withdrawn. Thus, claims 1, 5-7, 9-14, 27, 28, 30, and 39 are pending and subject to examination on the merits.

II. Claim Objections

Claims 47 and 48 are objected to by the Examiner, because "the word 'the' should be inserted prior to 'enzyme' in the phrase 'wherein enzyme is a glycosyltransferase.'" Applicants have inserted the word "the" as suggested by the Examiner. Thus, Applicants respectfully request withdrawal of this ground of objection.

III. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 1, 2, 5-13, 18-20, 26-28, 30, 39, 47, and 48 stand rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. Each ground of rejection under Section 112, second paragraph is addressed below.

A. Claims 1 and 48

Claims 1 and 48 stand rejected under 35 U.S.C. 112, second paragraph, because "the recitation of 'producing an oligosaccharide comprising lactose ... starting with at least one internalized exogenous precursor selected from the group consisting of lactose, sialic acid, α-galactoside, and β-galactoside' as it is unclear how sialic acid, α-galactosides or β-galactosides other than lactose are precursors for an oligosaccharide comprising lactose."

While not acquiescing in the propriety of the rejection, Applicants have amended claims 1 and 48 to no longer recite the phrase deemed unclear. Thus, the amendment renders this ground of rejection moot.

B. Claims 1, 2, 47, and 48

Claims 1, 2, 47, and 48 stand rejected for reciting "lacks any enzymatic activity liable to degrade said oligosaccharide, said precursor, and said intermediates" or "lacks any enzymatic activity liable to degrade said endogenous precursor."

While not acquiescing in the propriety of the rejection, Applicants have amended claims 1, 2, 47, and 48 to no longer recite the phrases identified by the Examiner. Thus, the amendment renders this ground of rejection moot.

C. Claim 47

Claims 47 stands rejected for reciting "oligosaccharide selected from the group consisting of lactose, sialic acid, α-galactoside, and β-galactoside," because "these are the exogenous precursor not the oligosaccharide to be synthesized."

While not acquiescing in the propriety of the rejection, Applicants have amended claim 47 to no longer recite the phrase identified by the Examiner. Thus, the amendment renders this ground of rejection moot.

D. Claims 47 and 48

Claims 47 and 48 stand rejected, because antecedent basis is allegedly lacking for "said intermediates."

While not acquiescing in the propriety of the rejection, Applicants have amended claims 47 and 48 to no longer recite "said intermediates." Thus, the amendment renders this ground of rejection moot.

E. Claims 20, 47, and 48

Claims 20, 47, and 48 stand rejected for reciting "exposing said cell to lactose permease under conditions sufficient to induce internalization of said exogenous precursor" and "wherein transport of said precursor is preformed by lactose permease," because "it is unclear under what conditions lactose permease will internalize sialic acid."

While not acquiescing in the propriety of the rejection, Applicants have amended claims 47 and 48 to no longer recite sialic acid as a precursor. Claim 20 has been canceled. Thus, the amendment renders this ground of rejection moot.

IV. Claim Rejections – 35 U.S.C. § 112, First Paragraph

A. Written Description

Claims 1, 2, 5-13, 18-20, 26-28, 30, 39, 47, and 48 stand rejected under 35 U.S.C. § 112, first paragraph, because "claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Office Action at 4-5. Applicants respectfully traverse this ground of rejection.

While not acquiescing in the propriety of the rejection, Applicants have amended the claims. Specifically, the claims now recite "lactose" as the only "exogenous precursor." The claims also specify that the E. coli is Z^-Y^+. Finally, the claims have been amended to more clearly define the culturing. Thus, the claims have been amended to more closely confirm with the working examples.

As amended, the claims directed to a method for producing an oligosaccharide comprising lactose using a genetically modified Z^-Y^+ *E. coli* cell. The cell comprises "at least one recombinant gene encoding an enzyme capable of modifying said exogenous precursor or one of the intermediates in the biosynthetic pathway of said oligosaccharide." This method allows for the production of oligosaccharides in high yield and avoids the use of organic solvents to increase membrane permeability. *See* spec. at page 11, ll. 6-10; page 15, ll. 9-11.

As discussed in detail in Applicants' responses of December 28, 2006 and February 28, 2007, the specification provides a complete description of the presently claim invention. For example, the specification describes the types of precursors that may be used, the genotypes of suitable cells, and synthetic routes to prepare specific oligosaccharides. This teachings is supplemented by actual working examples. Thus, the specification demonstrates that Applicants had possession of the claimed invention.

The Examiner states that "[t]he claims . . . recite a . . . enormously diverse genus of different methods each of which require different genes, ***different precursors*** and different modifications of the E. coli cell to prevent ***degradation of the precursors, intermediates and products*** and produce different end products." Office Action at 8 (emphasis added). However, the claims now recite lactose as the precursor, and the claims no longer require the cell be modified to prevent enzymatic degradation. Moreover, the claims more closely comport with the working examples. Thus, the specification confirms that the Applicants had possession of what is claimed as of the filing date of the application.

The Examiner also states that "specification clearly does not teach sufficient representative species to allow a skilled artisan to produce any oligosaccharide comprising lactose as the specification fails to teach enzymes and transporters necessary for utilization of many precursors of such oligosaccharides." Office Action at 6. However, the specification need not disclose what is already known in the art. The specification provides representative enzymes and transporters. Moreover, the specification provides working examples to demonstrate the use of the claimed invention. Because enzymes and transporters are known in the art, Applicants need not describe each and every one to satisfy the enablement requirement. Applicants need only demonstrate possession of the claimed invention, which has been done as discussed above.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

B. Enablement

Claims 1-13, 18-20, 25-28, 30, 39, 47, and 48 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. According to the Examiner, the specification "does not reasonably provide enablement for methods of making any oligosaccharide comprising lactose from lactose, sialic acid, any α-galactoside, or any β-galactoside in any E. coli." Office Action at 8-9. Applicants respectfully traverse this ground of rejection.

While not acquiescing in the propriety of the rejection, Applicants have amended the claims. Specifically, the claims now recite "lactose" as the only "exogenous precursor." The claims also specify that the *E. coli* is Z^-Y^+. Finally, the claims have been amended to more clearly define the culturing. Thus, the claims have been amended to more closely confirm with the working examples. In addition, the claims have been amended to more closely comport with the Examiner's view of enabled subject matter as set forth on page 8 of the Office Action.

The specification contains sufficient guidance to make and use the claimed invention without undue experimentation. For example, the specification contains working examples employing "lactose" as the only "exogenous precursor" and E. coli that is Z^-Y^+ as the genetically modified cell. Moreover, the specification contains a lengthy list of enzymes and genetic modifications that can be employed to practice the claimed invention. In view of this guidance, one of skill in the art could make and use the claimed invention without undue experimentation.

The Examiner argues that *In re Cook*, 439 F.2d 730 (CCPA 1971) does not apply to the present case, because in "*In re Cook* the court found that although the applicant had not taught those skilled in the art how to design an entire new zoom lens in short order, it has taught those skilled in the art how to design a new zoom lens of the type claimed in that case." Office Action at 12. However, the applicant in *In re Cook* claimed "an optical objective of the zoom type," *i.e.*, a zoom lens, comprising members having specified numerical relationships. *Id.* at 731. Thus, the applicant was claiming no all zoom lenses but those with members having the recited numerical relationship. As in *In re Cook*, Applicants are not claiming a method of producing *any* oligosaccharide using *any* cell. Instead, Applicants are claiming a "method for producing an oligosaccharide comprising lactose by a genetically modified cell starting with at least one internalized exogenous precursor consisting of lactose." The method employs a specific type of cell with specific modifications, and the method employs a specific culture technique. Applicants have enabled this claimed method, as evinced by the working examples demonstrating the use of the claimed invention.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

IV. Claim Rejections – 35 U.S.C. § 103

A. Bettler in view of Kozumi

Claims 1, 2, 5-13, 18-20, 26-28, 39, 47 and 48 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Bettler in view of Kozumi. Applicants respectfully traverse this ground of rejection.

As discussed in Applicants' December 28th and February 28th amendments, one of skill in the art would have no motivation to combine Bettler and Kozumi, much less any expectation of success, because it was known in the art that rapid uptake of sugars by lactose permease disrupts membrane function, possibly by causing collapse of the membrane potential. This phenomenon, which results in growth inhibition and eventually cell death, is known as "lactose killing." Given this knowledge in the art, a skilled artisan would have no reason to combine the teachings of Bettler and Kozumi, much less have an expectation of success.

The Examiner states that "a skilled artisan would merely have found it obvious to simply allow the cells to grow in the absence of inducer until a desired cell density is achieved and then add the inducer only during the oligosaccharide synthesis step and to keep the amount of inducer low such that lactose killing would be avoided." Office Action at 17. The claims now recite, however, that the precursor is added during "a second phase of cell growth limited by said carbon-based substrate which is added continuously." Neither Bettler nor Kozumi suggest such a step. Moreover, one of skill in the art would expect such a step to result in cell death. Even if one of skill in the art were to consider "allow[ing] the cells to grow in the absence of inducer until a desired cell density is achieved and then add the inducer only during the oligosaccharide synthesis step," this thought would be dismissed, because one of skill in the art would not expect that sufficient yields of oligosaccharide could be obtained while avoiding lactose killing.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

B. Bettler in view of Kozumi in further view of Johnson and Gotschlich

Claim 30 stands rejected under 35 U.S.C. § 103 as allegedly obvious over Bettler in view of Kozumi in further view of Johnson and Gotschlich. Applicants respectfully traverse this ground of rejection.

Bettler in view of Kozumi do not teach or suggest the claimed invention, as discussed above, and Johnson and Gotschlich fail to remedy this deficiency. For at least this reason, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

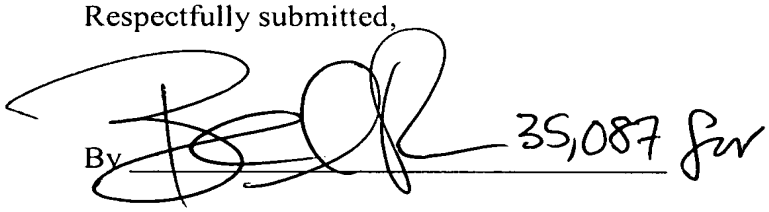
CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,



Date October 18, 2007

By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264